



US006322819B1

(12) **United States Patent**  
**Burnside et al.**

(10) **Patent No.:** **US 6,322,819 B1**  
(45) **Date of Patent:** **\*Nov. 27, 2001**

(54) **ORAL PULSED DOSE DRUG DELIVERY SYSTEM**

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(\*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/176,542**

(22) Filed: **Oct. 21, 1998**

(51) **Int. Cl.<sup>7</sup>** ..... **A61K 9/16**

(52) **U.S. Cl.** ..... **424/494; 424/472; 424/480**

(58) **Field of Search** ..... 424/494, 457, 424/471, 472, 480, 497, 461, 462, 470, 458, 459, 460, 468, 482

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

4,723,958 2/1988 Pope et al. .... 604/890.1  
4,871,549 10/1989 Ueda et al. .  
4,891,230 1/1990 Geoghegan et al. .... 424/461

(List continued on next page.)

**FOREIGN PATENT DOCUMENTS**

87/00044 1/1987 (WO) .  
90/09168 8/1990 (WO) .

**OTHER PUBLICATIONS**

Conte, et al., "Press-coated tablets for time-programmed release of drugs," *Biomaterials*, 14(13):1017-1023 (1993).  
Gazzaniga, et al., "Time-dependent oral delivery systems for colon targeting," *S.T.P. Pharma Sciences*, 5(1):83-88 (1995).

Gazzaniga, et al., "Oral Chronotopic Drug Delivery Systems: Achievement of Time and/or Site Specificity," *Eur. J. Pharm. Biopharm*, 40(4):246-250 (1994).

Pozzi, et al., "The Time Clock system: a new oral dosage form for fast and complete release of drug after a predetermined lag time," *Journal of Controlled Release*, 31:99-108 (1994).

Walia, et al., "Preliminary Evaluation of an Aqueous Wax Emulsion for Controlled-Release Coating," *Pharmaceutical Development and Technology*, 3(1):103-113 (1998).

Wilding, et al., "Gastrointestinal Transit and Systemic Absorption of Captopril from a Pulsed-Release Formulation," *Pharmaceutical Research*, 9(5):654-657 ((1992).

Xin Xu and Pink I. Lee, "Programmable Drug Delivery from an Erodible Association Polymer System," *Pharmaceutical Research*, 10(8):1144-1152 (1993).

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(57) **ABSTRACT**

A multiple pulsed dose drug delivery system for pharmaceutically active amphetamine salts, comprising an immediate-release component and an enteric delayed-release component wherein (1) the enteric release coating has a defined minimum thickness and/or (2) there is a protective layer between the pharmaceutically active amphetamine salt and the enteric release coating and/or (3) there is a protective layer over the enteric release coating. The product can be composed of either one or a number of beads in a dosage form, including either capsule, tablet, or sachet method for administering the beads.

**24 Claims, 8 Drawing Sheets**

